REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the following comments.

Claims 13-15, 17 and 23-26 are pending in the present application.

Applicants affirm election of the specie, fatigue, for examination of the present claims.

Claims 13-15, 17 and 23-26 stand rejected under 35 U.S.C. § 103(a) over the combination of five cited prior art references: Collins, et al., Kutilek et al., Wilder et al., Bull et al. and Shafron et al. The Examiner relies on the primary reference as teaching the use of a COX II inhibitor in the treatment of chronic fatigue syndrome or the side effects from radiation treatment. The Examiner acknowledges that the primary reference does not teach or suggest that COX II inhibitors are useful in the treatment of fatigue associated with radiation therapy, but asserts that its use therefor would have been obvious when the teachings of the secondary references are combined with Collins et al.

The Examiner also asserts that it is common knowledge that fatigue is mediated by the inflammatory process, but does not explain whether the fatigue referred to is fatigue associated with radiation therapy and does not cite any reference to support her contention.

Kutilek is relied upon as teaching that fatigue is a side effect of radiation treatment. Bull is relied on as teaching that fatigue, fever and chills are signs of inflammation and can be treated by treating inflammation. Wilder and Shafron are relied on as each teaching the effectiveness of COX II inhibitors and the use of COX II to treat radiation induced inflammation and fever, chills and fatigue.

The Examiner concludes, therefore, that the combination of cited prior art renders the use of COX II inhibitors to treat fatigue associated with radiation treatment obvious.

Applicants respectfully disagree with the Examiner's conclusion.

As noted above, the Examiner has not provided any evidence for her conclusion that fatigue associated with radiation therapy is mediated by an inflammatory response. Indeed, Applicants are aware of no data showing such a correlation. To the contrary, the source of fatigue in radiation therapy remains a scientific enigma to those of skill in the art. See, *e.g.*, Jaconsen and Thors, Seminars in radiation oncology, vol. 13, No.3, 2003, pp. 372-380 (copy enclosed). In that article, several factors that *may* be responsible for fatigue are discussed (pp. 376-377), such as pain, infections, dehydration, malnutrition, diarrhea, sleep disturbance, concurrent use of medications that commonly produce fatigue, anemia, depression and cytokine production. The authors discuss these factors in detail, and suggest that anemia is a likely common source of fatigue in radiation therapy patients. However, the inflammatory response, even an inflammatory response to infections, is not suggested as a source of fatigue.

In another study undertaken to determine the source of fatigue in radiation therapy patients, elevated levels of cytokines (including IL-1) were ruled out as a source of fatigue. Geinitz, et. al., Int. J. Radiation Oncol. Biol. Phys., vol. 51(3), 2001, pp. 691-8. The authors of this study concluded that the source of fatigue is unknown, but were able to rule out several factors, including elevated cytokines. An inflammatory response, *per se*, was not even considered in this study as a possible source of radiation-therapy fatigue.

Without evidence of a causal relationship between an inflammatory response and the fatigue associated with radiation therapy, the Examiner has failed to establish a *prima facie* case of obviousness. The secondary references relied on by the Examiner do not provide such evidence.

The Examiner relies on the primary reference, Collins et al., as teaching that a COX II inhibitor may be used to treat the side effects of radiation therapy that are mediated by an inflammatory response, and points to a recitation of chronic fatigue syndrome as such a condition. However, chronic fatigue syndrome and radiation-therapy induced fatigue are not even remotely related conditions. The Examiner has made an enormous leap from Collins et al.'s recitation of chronic fatigue syndrome to fatigue associated with radiation therapy based on an unfounded assertion that both types of fatigue are mediated by inflammation, when there is no evidence to support this, and indeed, the scientific literature quite clearly refutes the Examiner's assertion. Moreover, the secondary references relied on by the Examiner do not support this contention.

The secondary references relied on by the Examiner merely teach that fatigue is a side effect of radiation therapy, and that fatigue associated with inflammation can be treated with various agents, including COX II inhibitors. However, as noted above, there is no showing in any of the four cited prior art references that fatigue associated with radiation therapy is mediated by inflammation. Thus, in the absence of any teaching that the source of fatigue associated with radiation-therapy is mediated by an inflammatory response, the person of skill in the art would not be motivated to combine the cited prior art references in the manner suggested by the Examiner and would not, therefore, conclude that the present invention was obvious.

It is respectfully submitted that the rejection of claims 13-15, 17 and 23-26 under 35 U.S.C. § 103(a) over the combination of five prior art references is respectfully traversed.

It is also submitted that the present application is in condition for allowance, an early notification thereof being earnestly solicited.

Please charge any shortage in fees due in connection with the filing of this paper, including any extension of time fees, to Deposit Account 500417 and please credit any excess fees to such account.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 500417 and please credit any excess fees to such deposit account.

Respectfully submitted,

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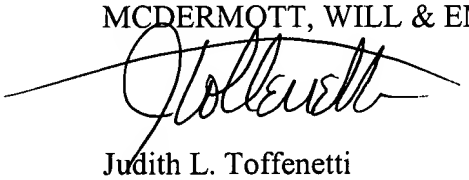

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